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     (FILE 'HOME' ENTERED AT 13:58:09 ON 07 NOV 2006)

     FILE 'DISSABS, 1MOBILITY, AGRICOLA, AQUASCI, BIOTECHNO, COMPENDEX,
     COMPUAB, CONFSCI, ELCOM, HEALSAFE, IMSDRUGCONF, INSPEC, LIFESCI, OCEAN,
     PAPERCHEM2, PASCAL, POLLUAB, SOLIDSTATE, ADISCTI, ADISINSIGHT, ADISNEWS,
     ANABSTR, ANTE, AQUALINE, BIOENG, BIOSIS, ...' ENTERED AT 13:58:25 ON 07
     NOV 2006
L1        320655 S (ALPHA (A) 4) OR ALPHA4 OR A4 OR (VLA (A)A) OR VLA4
L2         12230 S CD29
L3           289 S (L2 OR L1) (S) ( MULTIPLE MYELOMA)
L4            17 S L3 (S) ( IL (A) 6)
L5            11 DUP REM L4 (6 DUPLICATES REMOVED)
L6           272 S L3 NOT L4
L7           208 DUP REM L6 (64 DUPLICATES REMOVED)
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WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Tuesday, November 07, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ		
☐	L3	L1 same (multiple myeloma)	34
☐	L2	L1 same (MM or multiple myeloma)	7271
☐	L1	(alpha adj 4) or a4 or (vla adj 4)	171574

END OF SEARCH HISTORY

L5 ANSWER 11 OF 11 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
ACCESSION NUMBER: 1992:22332064 BIOTECHNO
TITLE: Characterization of adhesion molecules on human myeloma cell lines
AUTHOR: Uchiyama H.; Barut B.A.; Chauhan D.; Cannistra S.A.; Anderson K.C.
CORPORATE SOURCE: Division of Tumor Immunology, Dana-Farber Cancer Institute, 44 Binney St,Boston, MA 02115, United States.
SOURCE: Blood, (1992), 80/9 (2306-2314)
CODEN: BLOOAW ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB In multiple myeloma, malignant plasma cells are localized in marrow and rarely circulate in peripheral blood. To investigate the role of adhesion proteins in this process, we determined the expression and function of adhesion molecules on cell lines derived from patients with myeloma. The U266, ARH-77, IM-9, and HS-Sultan cell lines strongly expressed β1 and . alpha.4 integrins (89% to 98% positive), confirming that VLA-4 is the principal integrin on these cell lines. The U266 and IM-9 cell lines also expressed α.sub.3 integrin on 15% to 20% cells. In contrast, all lines lacked cell surface α2, α5, and α6 integrin expression (<5% positive). These cell lines adhered to fibronectin (20% to 40% specific binding), without significant binding to either collagen or laminin. Adhesion of these cell lines to fibronectin was partially blocked with either anti-β1 integrin monoclonal antibody (MoAb) (75% inhibition), anti-.alpha.4 integrin MoAb (75% inhibition), or RGD peptide (50% inhibition), but was unaffected by anti-αvβ3 or anti- αIIbβ3 MoAbs. Moreover, the combination of anti-β1 plus RGD peptide or anti-.alpha.4 plus RGD peptide inhibited binding to fibronectin by 80% and 95%, respectively. Finally, pretreatment and coculture of the IM-9 cell line with interleukin-6 (IL-6) resulted in a 52% decrease in specific binding to fibronectin (30% ± 6% to 15% ± 6%; P = .001), associated with a decrease in the number of cells expressing VLA-4 and a decrease in intensity of VLA-4 expression. These data suggest that myeloma cells adhere to fibronectin through VLA-4 as well as through RGD-dependent mechanisms, and that this binding can be downregulated by IL-6. Future studies of binding of both myeloma cell lines and freshly isolated tumor cells to extracellular matrix proteins and to marrow stroma may enhance our understanding of localization and trafficking of cells within the bone marrow microenvironment.

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RGD-dependent mechanisms, and that this binding can be downregulated by IL-6. Future studies of binding of both myeloma cell lines and freshly isolated tumor cells to extracellular matrix proteins and to. . .

ANSWER 9 OF 11 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN

ACCESSION NUMBER: 1994121051 ESBIOBASE
TITLE: Cell surface expression and functional significance of adhesion molecules on human myeloma-derived cell lines
AUTHOR: Kim I.; Uchiyama H.; Chauhan D.; Anderson K.C.
CORPORATE SOURCE: Dr. K.C. Anderson, Division Hematologic Malignancies, Dana-Farber Cancer Institute, Boston, MA 02115, United States.
SOURCE: British Journal of Haematology, (1994), 87/3 (483-493)
CODEN: BJHEAL ISSN: 0007-1048
DOCUMENT TYPE: Journal; Article
COUNTRY: United Kingdom
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Multiple myeloma is characterized by the presence of malignant plasma cells predominantly localized in bone marrow. Our prior studies have suggested that human myeloma derived-cell lines adhere specifically to fibronectin and to bone marrow stromal cells (BMSCs) via β1 and β2 integrins as well as RGD peptide, and that tumour cell to BMSC contact triggers interleukin-6 (IL-6) secretion from BMSCs. Since IL-6 is a growth factor for myeloma. adhesion may be important in paracrine IL-6 mediated tumour cell growth. We therefore examined phenotypic expression of adhesion molecules on the U266 and IM-9 human myeloma-derived cell lines using the panel of monoclonal antibodies (MoAbs) directed at adhesion molecules submitted to the Vth International Conference on Human Leukocyte Differentiation Antigens. U266 and IM-9 myeloma cell lines express mainly CD29. CD49d, VLA-1, CD18, CD54, ICAM-2 and ICAM-3. In contrast, CD49b, VLA-3, CD49f, CD11b, VCAM-1, selectins and selectin-ligands were not expressed on these cell lines. Specific adherence of IM-9 cells to BMSC line LP101 was demonstrated which could be partially blocked by pre-incubation and culture of tumour cells with anti-β1 integrin, anti-β2 integrin, anti-CD49d, anti-VLA-5, anti-CD11a, anti-CD44 and anti-CD54 MoAbs. The combination of these MoAbs (anti-CD29, CD18, CD11a, CD49d, VLA-5, CD44, CD54, ICAM-2, ICAM-3 MoAbs) decreased but did not completely abrogate binding of IM-9 to BMSCs. Moreover, increases in IL-6 secretion from BMSCs after adherence of IM-9 cells were also partially blocked by these MoAbs. These findings suggest that multiple adhesion pathways may mediate adherence of myeloma cell lines to BMSCs, localizing tumour cells in the marrow microenvironment and triggering IL-6 secretion by BMSCs which may augment tumour cell growth.

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L5 ANSWER 7 OF 11 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
DUPLICATE

ACCESSION NUMBER: 1994:24296388 BIOTECHNO
TITLE: Primary tumor cells of myeloma patients induce interleukin-6 secretion in long-term bone marrow cultures
AUTHOR: Lokhorst H.M.; Lamme T.; De Smet M.; Klein S.; De Weger R.A.; Van Oers R.; Bloem A.C.
CORPORATE SOURCE: Department of Haematology, University Hospital Utrecht, PO Box 85.500,3508 GA Utrecht, Netherlands.
SOURCE: Blood, (1994), 84/7 (2269-2277)
CODEN: BLOOAW ISSN: 0006-4971
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Long-term bone marrow cultures (LTBMC) from patients with multiple myeloma (MM) and normal donors were analyzed for immunophenotype and cytokine production. Both LTBMC adherent cells from myeloma and normal donor origin expressed CD10, CD13, the adhesion molecules CD44, CD54, vascular cell adhesion molecule 1, very late antigen 2 (VLA-2), and VLA-5, and were positive for extracellular matrix components fibronectin, laminin, and collagen types 3 and 4. LTBMC from myeloma patients and normal donors spontaneously secreted interleukin-6 (IL-6). However, levels of IL-6 correlated with the stage of disease; highest levels of IL-6 were found in LTBMC from patients with active myeloma. To identify the origin of IL-6 production, LTBMC from MM patients and normal donors were cocultured with BM- derived myeloma cells and cells from myeloma cell lines. IL-6 was induced by plasma cell lines that adhered to LTBMC such as ARH-77 and RPMI-8226, but not by nonadhering cell lines U266 and FRAVEL. Myeloma cells strongly stimulated IL-6 secretion in cocultures with LTBMC adherent cells from normal donors and myeloma patients. When direct cellular contact between LTBMC and plasma cells was prevented by tissue-culture inserts, no IL-6 production was induced. This implies that intimate cell-cell contact is a prerequisite for IL-6 induction. Binding of purified myeloma cells to LTBMC adherent cells was partly inhibited by monoclonal antibodies against adhesion molecules VLA-4, CD44, and lymphocyte function-associated antigen 1 (LFA-1) present on the plasma cell. Antibodies against VLA-4, CD29, and LFA-1 also inhibited the induced IL-6 secretion in plasma cell-LTBMC cocultures. In situ hybridization studies performed before and after coculture with plasma cells indicated that LTBMC adherent cells produce the IL-6. These results suggest that the high levels of IL-6 found in LTBMC of MM patients with active disease are a reflection of their previous contact with tumor cells in vivo. These results provide a new perspective on tumor growth in MM and emphasize the importance of plasma cell-LTBMC interaction in the pathophysiology of MM.

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ANSWER 208 OF 208 DGENE COPYRIGHT 2006 The Thomson Corp on STN
ACCESSION NUMBER: AAA11701 DNA DGENE
TITLE: Treating multiple myeloma and myeloma-induced bone reabsorption using antagonists of the alpha4/alpha4 integrin ligand pathway -
INVENTOR: Mundy G R; Yoneda T
PATENT ASSIGNEE: (BIOJ)BIOGEN INC.
PATENT INFO: WO 2000015247 A2 20000323 54
APPLICATION INFO: WO 1999-US21170 19990913
PRIORITY INFO: US 1998-100182 19980914
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-271253 [23]
DESCRIPTION: Murine VCAM-1 5' PCR primer.

AB This invention describes novel methods for treating multiple myeloma and myeloma-induced bone reabsorptions, comprising using integrin antagonists to disrupt the alpha4 integrin/ alpha4 integrin ligand pathway in vivo to reduce the capacity of the myeloma cells to survive and proliferate. The products of the invention have cytostatic and osteopathic activity. The antagonists inhibit the binding of alpha4 integrin and alpha4 integrin ligands which reduces the capacity of myeloma cells to proliferate and survive. The methods may be used for treating multiple myeloma, inhibiting the release of bone-reabsorbing factors by myeloma cells (which result in severe bone loss, the major side effect of myeloma in humans) and other disorders associated with osteoclastogenesis. This sequence represents a PCR primer used in the amplification of the murine VCAM-1 gene which is used to illustrate the method of the invention.

TI Treating multiple myeloma and myeloma-induced bone reabsorption using antagonists of the alpha4/alpha4 integrin ligand pathway -

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